



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/674,586	09/29/2003	Yu Zong Chen	069354.0103	5407

6449 7590 03/16/2006

ROTHWELL, FIGG, ERNST & MANBECK, P.C.  
1425 K STREET, N.W.  
SUITE 800  
WASHINGTON, DC 20005

EXAMINER

NEGIN, RUSSELL SCOTT

ART UNIT

PAPER NUMBER

1631

DATE MAILED: 03/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/674,586	<b>Applicant(s)</b> CHEN ET AL.	
	<b>Examiner</b> Russell S. Negin	<b>Art Unit</b> 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 21 December 2005.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) 22-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3, 5, 10-12, 14, 15, 19 and 21 is/are rejected.
- 7) ☒ Claim(s) 4, 6-9, 13, 16-18 and 20 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>2/11/05, 5/19/04</u> . | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's election of claims 1-21 (Invention I) in the reply filed on December 21, 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 22-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on December 21, 2005.

### ***Specification***

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. There are hyperlinks on page 17.

The disclosure is objected to because of the following informalities: One line 22, page 3 there is a spelling error. The word "theoretical" is incorrectly written.

Appropriate correction is required.

### ***Claim Objections***

Claims 1, 7, 8, 9, and 14 are objected to because of the following informalities:

There are nouns that should exist as plurals within the claim. In claim 1, line 5, the phrase "constructing at least one set of binding and reaction equation" should be "at least one set of binding and reaction equations." In claims 7-9, "at one or more connection point" should be "at one or more connection points." In claim 14, "at least one set of equation" should be "at least one set of equations." Appropriate correction is required.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-2, 10-12, and 14-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klaffke et al. [WO 02/08839] in view of Saltz et al. [USPAT 3,869,666].

Claims 1-2, 10, 12, 14-15 and 21 state:

1. A method for simulation of at least one biological and/or chemical reaction pathway comprising:
  - preparing a map of at least one biological and/or chemical reaction pathway;
  - constructing at least one set of binding and reaction equation from the pathway map;
  - constructing at least one set of concentration equation for molecules of the pathway map;

Art Unit: 1631

constructing an electronic circuit corresponding to every set of equation; and  
determining simulation of pathway by measuring voltage at two or more  
connection points of the circuit.

2. The method of claim 1, wherein the binding, reaction and/or concentration equation is a linear or non-linear first- or second-order ordinary differential equation (ODE).

10. The method of claim 1, wherein the biological pathway comprises at least one object, and wherein the object is protein, nucleic acid, ligand, substrate, inhibitor or antagonist, activator or agonist, reactant and/or reaction product.

11. An electronic circuit system for the simulation of at least one biological and/or chemical reaction pathway, comprising at least one electronic circuit representing a set of binding, reaction and/or concentration equation.

12. The electronic circuit system of claim 11, wherein the binding, reaction and/or concentration equation is a linear or non-linear first- or second-order ordinary differential equation (ODE).

14. A method for molecular dynamics simulation of biomolecules and/or nano-molecular systems comprising:

constructing at least one set of equation representing the molecular dynamics of at least one molecule of the biomolecules and/or the nano-molecular systems;  
constructing an electronic circuit representing every set of equation; and  
determining molecular dynamics simulation by measuring voltage at two or more connection points of the circuit.

15. The method of claim 14, wherein the equation is a linear or non-linear second order ordinary differential equation (ODE).

21. The method of claim 14, wherein the biomolecule comprises amino acids, nucleotides and/or organic molecules.

Klauffe et al. teach a "method for simulating chemical reactions." Page 23 shows a chemical reaction to be simulated. Page 25 shows a binding reaction of hydrogen sulfide ligand binding to a sugar (an organic molecule). Page 8, lines 15-20 illustrate a set of concentration equations for the binding pathway in terms of a linear, ordinary differential equation. Solving these equations is a study in molecular dynamics.

Klauffke et al. fail to show how circuitry accounts for simulation of these reactions.

Saltz et al. state in their abstract, "An instrument and method for obtaining the maximum slope of a function such as a sigmoidally shaped curve... The disclosed instrument when used in conjunction with conventional converters is ideally suited for reaction rate measurements frequently encountered in the kinetic analysis of enzymes, or in any other chemical reaction which follows a sigmoidally shaped curve and where reliability in determining the point of maximum slope in a minimum time is critical." Saltz et al. show a picture of such a circuit with a voltmeter for measuring voltage in the circuit, which more expediently calculates reaction parameters than manual methods.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the method of Klauffke et al. by use of the apparatus of Saltz et al. because Saltz et al. use electric circuitry to analyze the kinetics of enzymes in a way that is an improvement by being more expedient than existing manual and microcomputer methods while remaining inexpensive.

Claims 1 and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klauffke et al. in view of Saltz et al. as applied to claims 1-2, 10-12, and 14-15 above, and further in view of Fussenegger et al [Nature Biotechnology, volume 18, 2000, pages 768-774].

Claims 1 and 3 state:

1. A method for simulation of at least one biological and/or chemical reaction pathway comprising:
  - preparing a map of at least one biological and/or chemical reaction pathway;
  - constructing at least one set of binding and reaction equation from the pathway map;

Art Unit: 1631

constructing at least one set of concentration equation for molecules of the pathway map;

constructing an electronic circuit corresponding to every set of equation; and determining simulation of pathway by measuring voltage at two or more connection points of the circuit.

3. The method of claim 1, wherein the binding, reaction and/or concentration equation is a non-linear first-order ordinary differential equation (ODE).

While the method of the base claim of simulating chemical reactions are taught by Saltz and Klaffke, these two sources fail to teach the method of using non-linear first order differential equations.

Fussenegger et al. teach such a mathematical model such as equation 9 in the appendix on page 773, which is a first order non-linear differential equation used to model caspase function in apoptosis.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the apparatus of Saltz and the method of Klaffke as applied to claims 1-2, 10-12, and 14-15 by use of the mathematical model of Fussenegger because Fussenegger et al. teach how to apply non-linear first order differential equations to analyze enzyme kinetics.

Claims 1, 5, 14, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klaffke et al. in view of Saltz et al. as applied to claims 1-2, 10-12, and 14-15 above, and further in view of Zelina [USPAT 3,193,755].

Claims 1, 5, 14, and 19 state:

1. A method for simulation of at least one biological and/or chemical reaction pathway comprising:

preparing a map of at least one biological and/or chemical reaction pathway;

Art Unit: 1631

constructing at least one set of binding and reaction equation from the pathway map;

constructing at least one set of concentration equation for molecules of the pathway map;

constructing an electronic circuit corresponding to every set of equation; and determining simulation of pathway by measuring voltage at two or more connection points of the circuit.

5. The method of claim 1, further comprising maintaining the voltage level of the circuit between two fixed voltage values.

14. A method for molecular dynamics simulation of biomolecules and/or nano-molecular systems comprising:

constructing at least one set of equation representing the molecular dynamics of at least one molecule of the biomolecules and/or the nano-molecular systems;

constructing an electronic circuit representing every set of equation; and determining molecular dynamics simulation by measuring voltage at two or more connection points of the circuit.

19. The method of claim 14, further comprising maintaining the voltage level in the circuit between two fixed voltage values.

The limitations of claims 1 and 14 are taught in the apparatus of Saltz and the method of Klaffke as applied to claims 1-2, 10-12, and 14-15 which teach how to simulate a chemical reaction. However, neither source teaches upper and lower voltage limits on the circuitry.

Zelina teaches in column 1, lines 23-27, "Another object of this invention is to provide a circuit which senses any deviations in the voltage magnitude of a voltage beyond a predetermined range defined by maximum and minimum voltage levels."

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the apparatus of Saltz and the method of Klaffke as applied to claims 1-2, 10-12, and 14-15 because Zelina teaches the application of a voltage regulator, which would regulate voltage within a maximum and minimum level



Art Unit: 1631

and has the advantage of being a better controller of voltage through a circuit than other circuits without such regulators.

### ***Claims Objections***

Claims 4, 6-9, 13, 16-18, and 20 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

### ***Conclusion***

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, Ph.D., whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Ardin Marschel, Ph.D., Supervisory Patent Examiner, can be reached at (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Tina Plunkett, whose telephone number is (571) 272-0549.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

Application/Control Number: 10/674,586

Page 9

Art Unit: 1631

For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

-RSN 3/9/06

*JPB 3/9/06*

*John S. Brusca 9 March 2006*  
**JOHN S. BRUSCA, PH.D**  
**PRIMARY EXAMINER**